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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PIONEER HI-BRED INTERNATIONAL INC. 7100 N.W. 62ND AVENUE P.O. BOX 1000 JOHNSTON, IA 50131			EXAMINER	
			NELSON, AMY J	
		ART UNIT	PAPER NUMBER	
		1638		

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	08/963,096	ZHAO ET AL.
	Examiner Amy Nelson	Art Unit 1638

— The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 21 January 2003.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 90 and 91 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 90 and 91 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 21 January 2003 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 20 & 21.

4) Interview Summary (PTO-413) Paper No(s). _____.

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____.

DETAILED ACTION

1. The Double Patenting rejection has been withdrawn in view of the restriction requirement in parent Application Serial No. 08/788,018, as noted by applicant on p. 4 of the response filed 12/24/02.

Specification

2. The amendment filed 3/26/99 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment to replace “PHP28” with -PHP38- appears to introduce new matter into the specification. Applicant fails to point to support for the “PHP38” in the originally filed specification. Hence, the amendment appears to constitute new matter. Applicant is required to point to support for the amendment or to cancel the NEW MATTER in the reply to this Office Action.

Claim Rejections - 35 USC § 112

3. Claims 90 and 91 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transformed inbred maize plant PHJ90, PHN46, and PHP28(38) prepared by the disclosed PHI method, does not reasonably provide enablement for any and all inbred maize plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

The claims are drawn to an inbred maize plant other than A188 stably transformed with *Agrobacterium* comprising a nucleic acid. Applicant also claims seed produced by the maize plant.

Applicant teaches preparation of *Agrobacterium* vectors comprising the ubiquitin promoter operably linked to the GUS reporter coding DNA and the CaMV 35 S promoter operably linked to the BAR selectable marker coding DNA (Example 1). Applicant also teaches transformation of A188 and Hi-II (an F1 hybrid from a cross between A188 and B73) following the method of Ishida (Nature Biotech. 14: 745-750, 1996) (Examples 2 and 3; Tables 3 and 4). Applicant teaches transformation of Hi-II following their own (PHI) protocol, with or without a resting step, and teach an increased transformation efficiency with the PHI protocol as compared to the Ishida protocol, especially with the resting step (Examples 4 and 5; Tables 5-7). Applicant teaches transformation of F1 hybrid maize plants produced by crossing A188 with any of PHJ90, PHN46, or PHPP8, and shows that higher transformation efficiency is obtained than with the Ishida protocol (Example 6, Table 8). Finally, Applicant teaches transformation of three elite inbreds, PHJ90, PHN46, and PHP28(38) using the PHI

protocol, and teaches that none of the three inbreds could be successfully transformed with the Ishida protocol (Example 7, Table 9). Applicant discloses that gus positive events are present for each line at the callus and regenerated plant stage, and hence concludes that each of the lines has been stably transformed (p. 42-43).

Applicant does not teach transformation of other inbred maize lines encompassed by the claims other than PHJ90, PHN46, and PHP28(38), and Applicant does not teach seed of the transformed maize lines. Also, Applicant does not teach that the transformed plants are stably transformed. One of skill in the art would recognize that stably transformed maize plants would be progeny plants derived from the originally transformed line wherein the transgene is not lost, but remains in the genome. Applicant has not provided guidance for stably transformed inbred maize lines.

At the time of Applicant's invention, transformation of maize by *Agrobacterium* was very unpredictable, and only a few researchers reported successful transformation of monocotyledonous plants using *Agrobacterium*. Of the reported successes, "the transformation frequencies in these methods was rather low, and some of the studies did not provide sufficient molecular and genetic evidence of production of transgenic plants" (Ishida *et al.*, *Nature Biotech.* 14: 745-750, 1996, see p. 745, left-hand column).

Applicant teaches only that the PHI protocol allowed transformation of inbred lines PHJ90, PHN46, and PHP28(38), which could not be transformed using the prior art method of Ishida. However, the source of these three lines is unclear, and the relationship of the three lines to each other, to A188, and to other inbred maize lines as broadly claimed is unclear. Hence, one of skill in the art cannot easily determine if the PHI protocol would be expected to be universally applicable to all maize lines, or is

simply a preferable protocol for the three disclosed lines. Furthermore, Applicant does not provide guidance for *Agrobacterium* transformation of maize other than by the disclosed protocol. In the absence of such guidance, undue trial and error experimentation would be required to screen through a multitude of different protocols with varying parameters, using a myriad of different inbred maize lines from a variety of different parental sources, to determine how to transform all inbred maize plants by all possible *Agrobacterium* transformation methods. Hence, the claims should be limited in scope to plants produced by the disclosed method. It is unclear to the Examiner exactly which steps of the PHI protocol are critical to successful transformation of the three disclosed inbred lines, and are required for the unexpected results with the three lines over the method of Ishida. However, the scope of the claims should be limited to the scope of the teachings of unexpected results.

Finally, because Applicant teaches only gus positive T0 generation plants, it is not clear to the examiner that stably transformed plants were produced. Applicant argues in their response that proof of stable transformation requires evidence such as Southern blots, enzyme assay, and transmission to sexual offspring populations (response filed 12/24/02, p. 4). In the absence of evidence to the contrary, it is submitted that Applicant has not enabled “stably transformed” maize plants *per se*.

In conclusion, in view of the broad scope of the claims directed to any and all *Agrobacterium* transformed inbred maize plants and seeds, the unpredictability in the art of *Agrobacterium* transformation of maize, the limited guidance in the instant specification directed to only three maize inbred lines from unknown source using a particular PHI protocol and failing to teach stable transformation by way of transgenic

progeny plants, the significant amount of experimentation required to screen through a myriad of different transformation protocols with the multitude of different inbred lines, it is submitted that the claimed invention is not enabled.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 91 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is directed to a seed from the transformed maize plant. Due to segregation, all of the seed of any given transformed maize plant need not be transgenic. Hence, the claimed seed reads on untransformed maize seed, which is a product of nature and not one of the five classes of patentable subject matter. Amendment of the claim to recite –transformed- or –transgenic- would obviate the rejection.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 90 and 91 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldman *et al.* (U.S. Patent 5,177,010). This rejection is repeated for the reasons of record as set forth in the Official action mailed 9/3/02. Applicant's arguments filed 12/24/02 have been fully considered but they are not persuasive.

Goldman teaches transformed maize plants and seeds (abstract), including Iochief Maize plants and seeds (Examples 1, 2, 4, 5, 7-10), and C58 plants and seeds (Examples 3 and 6). Hence, all of the claim limitations have been previously disclosed by Goldman.

8. Claims 90 and 91 are rejected under 35 U.S.C. 102(e) as being anticipated by Goldman *et al.* (U.S. Patent 6,020,539).

Goldman teaches transformed maize plants and seeds (abstract), including Iochief Maize plants and seeds (Examples 1, 2, 4, 5, 7-11), and C58 plants and seeds (Examples 3 and 6). Hence, all of the claim limitations have been previously disclosed by Goldman.

Applicant asserts that the '010 patent (and consequently the '539 patent) are not enabling for a maize plant stably transformed with *Agrobacterium*. Applicant submits court decisions wherein the teachings of a Graves and Goldman article was discussed and determined to be nonenabling. Applicant argues that proof of stable transformation

requires evidence such as Southern blots, enzyme assay, and transmission to sexual offspring populations. No such evidence is shown in the '010 patent (response, p. 3-4).

Examiner is not in a position to question the validity of an issued patent. Both the '010 and the '539 patent have claims directed to methods of transforming maize or to transformed maize plants. The claims are not limited to transiently transformed maize plants, and hence the claims are presumed to encompass stably transformed maize plants. Moreover, Applicant's evidence of non-enablement of the Graves journal article is not germane to a discussion of enablement of an issued patent because enabling evidence may be provided post-filing date in a patent application. Therefore, the rejections are considered to be proper, and are maintained.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 90 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishida *et al.* (Nature Biotech. 14: 745-750, 1996).

Ishida teaches transformed maize plants and seeds, including A188 inbred maize plants and seeds as well as hybrid maize plants (A188 crossed with another inbred) and seeds (abstract). Ishida teaches inheritance of the marker genes in the progeny plants, and hence teaches that the plants are stably transformed (p. 747, left-hand column). Also, it is

noted that Applicant admits that the protocol of Ishida allows production of stably transformed maize plants (specification, p. 35, lines 14-16).

Ishida does not teach transformed inbred maize plants other than A188. However, it is would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the invention of Ishida to transform other inbred maize lines. The different inbred maize lines are functional equivalents and it would have been obvious to substitute one functional equivalent for another, in the absence of evidence to the contrary.

Applicant teaches the unsuccessful application of the method of Ishida to three particular inbred maize lines, and unexpected success with a modified transformation method. Hence, Applicant's claimed invention should be limited in scope to the teachings of unexpected results, *i.e.* the particular lines transformed and the method of transformation (or at least the critical method steps that allowed for successful transformation).

11. Claims 90 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hiei et al. (US Patent 5,591,616; filed 7/6/93).

Hiei teaches transformed maize plants and seeds, including A188 inbred maize plants and seeds as well as hybrid maize plants (A188 crossed with another inbred) and seeds (Example 2). Hiei teaches that the transformed calli and plants express gus.

Hiei does not teach transformed inbred maize plants other than A188. However, it is would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the invention of Hiei to transform other inbred maize lines. The different inbred maize lines are functional equivalents and it would have been

obvious to substitute one functional equivalent for another, in the absence of evidence to the contrary.

Applicant teaches the unexpected successful transformation of three particular inbred maize lines with a modified PHI transformation method. Hence, Applicant's claimed invention should be limited in scope to the teachings of unexpected results, *i.e.* the particular lines transformed and the method of transformation (or at least the critical method steps that allowed for successful transformation).

12. Any inquiry concerning this communication should be directed to Amy Nelson at telephone number (703) 306-3218. The examiner can normally be reached Monday-Friday from 8:30 am to 5:00 pm.

The fax phone number for TC 1600 is (703) 872-9306 (before final) or (703) 872-9307 (after final).

Any inquiry of a general nature, relating to the status of this application or if a paper has not been received, should be directed to TC 1600 Customer Service at (703) 308-0198.



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